REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Claim Amendments

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

Claims 13, 15, and 27-28 are requested to be cancelled, without prejudice or disclaimer thereof. Applicants note that the Office Action Summary sheet does not indicate that claims 13, 15, and 27-28 are pending.

Claims 3, 5-8, 11 and 51 are currently being amended to advance prosecution of this application. Support for amended claims 3, 5-8, 11, and 51 is provided in the specification and claims as originally filed, as further discussed below.

It is acknowledged that the foregoing amendments are submitted after final rejection of the claims. However, because the amendments do not introduce new matter, and either place the application in condition for allowance or at least in better condition for appeal, entry thereof by the Examiner is respectfully requested.

After entry of the amendments as set forth above, claims 3-9, 11 and 51 are pending in this application.

II. New Matter Rejection

Claims 3, 6, 7, 8 and 9 were rejected under 35 U.S.C. § 112, first paragraph, "as failing to comply with the written description requirement." The Examiner contends that the claims recite subject matter that "was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." In particular, the Examiner contends that the addition of the phrase "wherein the fragment has carbonic anhydrase activity or where the fragment has immunological activity of carbonic anhydrase" in claims 3, 6, 7, 8 and 9, "is not supported by the original disclosure." The Examiner asserts that TABLE 2 does not provide support for the limitation "has carbonic anhydrase activity" because TABLE 2 "merely describ[es] the activity of the closest homolog [and] not of the polypeptide of SEQ ID NO: 1." Applicants respectfully traverse this ground for rejection.

Applicants first note that "[t]he Examiner has the initial burden of presenting by a ***preponderance of evidence*** why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." MPEP § 2163.04 "Burden on the Examiner with Regard to the Written Description Requirement" (citing *In re Wertheim* 541 F.2d 257, 262 (CCPA 1976) (Emphasis added). The Examiner has not met the burden of establishing by a preponderance of evidence that a person skilled in the art would not recognize in Applicants' disclosure a description of the invention defined by the claims. The specification, as filed, fully supports the subject matter of the claims.

TABLE 2 lists SEQ ID NO: 1, and under the heading "GenBank Homolog" recites "[*Mus musculus*] carbonic anhydrase XIII" and "[*Homo sapiens*] carbonic anhydrase I." Reading TABLE 2, one skilled in the relevant art would recognize that TABLE 2 indicates that homologs of SEQ ID NO: 1 include *Mus musculus* carbonic anhydrase XIII and *Homo sapiens* carbonic anhydrase I. One skilled in the art would understand that the term "homolog" means "something homologous," and one skilled in the relevant art would understand that the term "homologous" means "similar in function." As such, reading TABLE 2, one skilled in the relevant art would understand that TABLE 2 indicates that the polypeptide of SEQ ID NO: 1 has a similar function as the recited carbonic anhydrases.

Therefore, TABLE 2 provides explicit support for the limitation "has carbonic anhydrase activity" with respect to SEQ ID NO: 1.

Moreover, in addition to the support provided in TABLE 2, the specification includes further support for the limitation "has carbonic anhydrase activity." For example, TABLE 3 lists SEQ ID NO: 1 and under the heading "Signature Sequences, Domains and Motifs" recites "Eukaryotic-type carbonic anhydrase domain: W6-A239...Eukaryotic-type carbonic anhydrases signature...Eukaryotic-type carbonic anhydrases signature: G82-A143...CARBONIC ANHYDRASE DEHYDRATASE...CARBONIC ANHYDRASE...Eukayotic carbonic anhdrases motif: S106-V122." As such, reading TABLE 3, one skilled in the relevant art would understand that TABLE 3 indicates that the polypeptide of SEQ ID NO: 1 includes "Signature Sequences, Domains and Motifs" that are characteristic of carbonic anhydrases. Therefore, TABLE 3 provides explicit support for the limitation "has carbonic anhydrase activity" with respect to SEQ ID NO: 1.

Finally, additional support for the limitation "has carbonic anhydrase activity" is also provided at paragraph **[0130]** of the specification, which states:

> SEQ ID NO:1 is 59% identical, from residue M1 to residue A239, to human carbonic anhydrase I (GenBank ID g179793) as determined by the Basic Local Alignment Search Tool (BLAST). (See Table 2.) The BLAST probability score is 6.9e-80, which indicates the probability of obtaining the observed polypeptide sequence alignment by chance. SEQ ID NO:1 also contains a eukaryotic-type carbonic anhydrase domain as determined by searching for statistically significant matches in the hidden Markov model (HMM)-based PFAM database of conserved protein family domains. (See Table 3.) Data from BLIMPS, MOTIFS, and PROFILESCAN analyses provide further corroborative evidence that ***SEQ ID NO:1 is a carbonic anhydrase.*** (Emphasis added.)

As such, with respect to the limitation "has carbonic anhydrase activity," the Examiner is incorrect in stating that the claims recite subject matter that "was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." The specification clearly conveys that SEQ ID NO: 1 "has carbonic anhydrase

activity" and provides "corroborative evidence that SEQ ID NO:1 is a carbonic anhydrase." *See, e.g.*, paragraph **[0130]**. Therefore, the limitation "has carbonic anhydrase activity" is not new matter, and Applicants request that the Examiner withdraw the rejection.

III. Written Description

Claims 11 and 51 were rejected under 35 U.S.C. § 112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." The Examiner noted that claims 11 and 51 recite polynucleotides or polypeptides which are 90% or 95% identical to SEQ ID NO: 4 or SEQ ID NO: 1, "with no defined function." Further, the Examiner asserts that SEQ ID NO: 1 has "62% homology" to enzymes such as gamma-phosphatase and beta-phosphatase. Applicants respectfully traverse the rejection for the following reasons.

Claim 3, from which claim 51 depends, has been amended to recite a polynucleotide encoding "a polypeptide comprising an amino acid sequence at least 90% identical to an amino acid sequence of at least about 20 contiguous amino acids of SEQ ID NO:1, wherein the polypeptide has carbonic anhydrase activity." Claim 11 has been amended to recite a "polynucleotide comprising a polynucleotide sequence at least 90% identical to a polynucleotide sequence of at least about 60 contiguous nucleotides of SEQ ID NO:4, wherein the polynucleotide encodes a polypeptide that has carbonic anhydrase activity." As such, the amended claims recite polynucleotides encoding polypeptides "with defined functions" related to carbonic anhydrase activity.

One skilled in the relevant art would recognize that Applicants were in possession of the claimed subject matter. First, just as there exists degeneracy of the DNA code, there similarly exists amino acid substitutions that can be made to a polypeptide, which are conservative in nature, and which do not alter the basic properties of the residue that is replaced. For instance, a glycine or a serine residue can replace an alanine residue. Applicants disclose at paragraphs **[0056]** – **[0057]** "conservative amino acid substitutions"

that can be made to a polypeptide sequence without disrupting function. *See* U.S. 2003-0121061, paragraphs **[0056-0057]**.

Applicants also teach various structural and functional domains of SEQ ID NO. 1. At TABLE 3, the specification indicates that SEQ ID NO: 1 includes "potential phosphorylation sites"; a "potential glycosylation site"; and "signature sequences, domains and motifs." *See* U.S. 2003-0121061, TABLE 3, paragraph **[0338]**. In addition, assays for determining the function and measuring the activity of carbonic anhydrases are known in the art. As such, one skilled in the art would recognize that Applicants, at the time of filing, were in possession of SEQ ID NO: 1 and SEQ ID NO: 4, as well as sequences ***related*** to SEQ ID NO: 1 and SEQ ID NO: 4.

Moreover, consistent with recent Federal Circuit ruling and M.P.E.P. guidelines, Applicants need not have provided explicit disclosure for each and every nucleic acid sequence that encodes a polypeptide of SEQ ID NO: 4. Specifically, the Federal Circuit has recently stated:

> The state of the art has developed such that the complete amino acid sequence of a protein may put one in possession of the genus of DNA sequences encoding it, and that one of ordinary skill in the art at the time the [application] was filed may have therefore been in possession of the entire genus of DNA sequence that can encode the disclosed [sequence], even if individual species within that genus might not have been described or rendered obvious....Moreover, we see no reason to require a patent applicant to list every possible permutation of the nucleic acid sequences that can encode a particular protein for which the amino acid sequence is disclosed, given the fact that it is, as explained above, a routine matter to convert back and forth between an amino acid sequence and the sequences of the nucleic acid molecules that can encode it.

See In re Wallach, 378 F.3d 1330, 1333-34 (Fed. Cir. 2004)(citations omitted).

In addition, the M.P.E.P. states:

> Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus

> embraces. For example, in the molecular biology arts, if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, but not necessarily any particular species.

See M.P.E.P. 2163.II.A.3.a.ii. (8th ed., rev. 2 2001)(citations omitted).

As such, Applicants need not have provided explicit disclosure for each and every nucleic acid sequence that encodes a polypeptide of SEQ ID NO: 4. Rather, because the specification discloses a polypeptide of SEQ ID NO: 1, one skilled in the art would recognize that Applicants were in possession of the genus of DNA sequences encoding SEQ ID NO: 1. For example, it is well known in the art that an amino acid may be encoded by more than one codon triplet. The genus of DNA sequences that may encode a full-length protein includes those sequences that are divergent by virtue of being degenerate in sequence.

As such, one skilled in the art would reasonably conclude that Applicants were in possession of the claimed invention at the time the application was filed. Applicants request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 112, first paragraph, for inadequate written description.

IV. Enablement Rejection

Claims 3, 6-9, 11 and 51 were rejected under 35 U.S.C. § 112, first paragraph, allegedly "because the specification, while being enabling for an isolated nucleic acid (or polynucleotide) sequence of SEQ ID NO: 4 encoding a specific lyase(?) or SEQ ID NO: 1, does not reasonably provide enablement for "any fragment [biologically active or immunogenic] of SEQ ID NO: 1 or 4; or that encoding a protein having 90% or 95% homology to SEQ ID NO: 1 or a nucleic acid having 90% similarity to SEQ ID NO: 4." Applicants thank the Examiner for indicating that the specification enables claims to an

isolated nucleic acid (or polynucleotide) of SEQ ID NO: 4 or SEQ ID NO: 1. Applicants respectfully assert that the claims are fully enabled and traverse the rejection for the following reasons.

Claim 3 has been amended to delete the limitations "biologically active fragment" and "immunogenic fragment." Further, as noted above, claims 3 and 11 have been amended to recite polynucleotides encoding polypeptides "with defined functions" related to carbonic anhydrase activity.

One skilled in the art would know how to make and use the sequences recited in the claims as amended. Carbonic anhydrases are well studied in the art and are known to catalyze the interconversion of CO_2 and HCO_3^-. *See* U.S. 2003-0121061, paragraph **[0005]**. Assays for measuring the activity of carbonic anhydrases are known in the art. *See* Lehtonen *et al.* As such, one skilled in the art would know how to identify specific catalytic amino acids and/or structural motifs essential for activity/function which must be preserved in an encoding polynucleotide without having to undertake "undue experimentation."

Further, Applicants teach various structural and functional domains of SEQ ID NO. 1. At TABLE 3, the specification indicates that SEQ ID NO: 1 includes "potential phosphorylation sites"; "potential glycosylation sites"; and "signature sequences, domains and motifs." *See* U.S. 2003-0121061, TABLE 3, paragraph **[0338]**. This information informs the skilled person of the pertinent portions and characteristics of the polypeptide sequence designated by SEQ ID NO. 1 and the polynucleotide sequence designated by SEQ ID NO: 4. Therefore, provided with this information, one skilled in the art would know which residues of SEQ ID NO. 1 and SEQ ID NO: 4 may be required for carbonic anhydrase activity.

In addition, as noted above, amino acid substitutions can be made within a polypeptide, which are conservative in nature and which do not alter the basic properties of the amino acid that is replaced. For instance, a glycine or a serine residue can replace an alanine residue. Applicants disclose at paragraphs **[0056]** – **[0057]** "conservative amino acid substitutions" that can be made to a polypeptide sequence without disrupting function. *See* U.S. 2003-0121061, paragraphs **[0056-0057]**.

Further, one skilled in the art, provided with a polypeptide sequence, would know how to make the entire genus of polynucleotide variants that could possibly encode that polypeptide, and that it is unnecessary to enable each and every one of those polynucleotide species. *See* discussion provided above with respect to the "written description requirement" and *In re Wallach*, 378 F.3d 1330, (Fed. Cir. 2004). For these reasons, the claims are fully enabled. Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement.

V. Utility

Claims 3-9, 11 and 51 were rejected under 35 U.S.C. § 101 allegedly because "the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility." Applicants respectfully traverse the rejection for the following reasons.

First, the Examiner asserts that the claims relate to "a family of Lyases, which is a generic asserted utility," and which does not satisfy the utility requirement. However, the amended claims specifically relate to ***carbonic anhydrases***. Further, the Examiner asserts that "one or [*sic*, of] ordinary skill in the art would not know which is a substrate for the enzyme." As indicated in the specification and discussed above, carbonic anhydrases catalyze the interconversion of CO_2 and HCO_3^-. *See* U.S. 2003-0121061, paragraph **[0005]**. One skilled in the relevant art would recognize that the interconversion of CO_2 and HCO_3^- is important for enumerable biochemical, physiological, and industrial processes. As such, carbonic anhydrases have a well established utility.

Furthermore, carbonic anhydrases may participate in a variety of specific and substantial physiological processes that involve pH regulation, CO_2 and HCO_2^- transport, ion transport, and water and electrolyte balance. *See* U.S. 2003-0121061, paragraph **[0006]**. A number of disease states are marked by variations in carbonic anhydrases activity, including osteopetrosis, disease activity related to brain damage, central nervous system infection, dementia, trigeminal neuralgia, colonic adenomas and adenocarcinomas, glaucoma, essential

tremor and Parkinson's disease, altitude related illnesses, hyperthyroid Graves' disease, diabetes mellitus, and endometriosis. *See* U.S. 2003-0121061, paragraphs **[0007]-[0009]**.

Subsequent to the filing of the present application, Lehtonen *et al.* confirmed that SEQ ID NO: 1 is 100% identical to amino acids 1-242 of a polypeptide termed "carbonic anhydrase XIII" or "CA XIII". *See* Lehtonen *et al.*, J BIOL. CHEM. 2004 Jan 23;279(4):2719-27, [hereinafter "Lehtonen"], at page 2722, (copy previously submitted with Information Disclosure Statement dated December 30, 2005). Lehtonen shows that CA XIII is expressed in a number of tissues including thymus, small intestine, spleen, prostate, ovary, colon, and testis. In mouse, positive tissues included the spleen, lung, kidney, heart, brain, skeletal muscle, and testis. *See id.* at pages 2721, and 2723-2726. Further, Lehtonen states that "the predicted amino acid sequence, structural model, distribution, and activity data suggest that CA XIII represents a novel enzyme, ***which may play important physiological roles in several organs***." *See id.* at page 2719. Lehtonen indicates that tests are underway to determine whether "CA XIII inhibition may constitute a new pharmacological target." *See id.* at page 2727. In particular, Lehtonen states that "[o]ne could hypothesize that CA XIII might contribute to normal fertilization process by producing the appropriate bicarbonate concentration in the cervical and endometrial mucus," and that "it would be interesting...to determine the role of this novel enzyme on spermatogenesis and fertilization capacity." *See id.* Therefore, Lehtonen, ***representing those of relevant skill in the art***, has suggested that the polypeptide of SEQ ID NO: 1 has a specific and substantial utility.

As such, the specification asserts a specific, substantial and well established utility for SEQ ID NO: 1, as described in the specification and as confirmed by Lehtonen. Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 101, for lack of utility.

VI. Claim Rejections – 35 U.S.C. § 112, Second Paragraph

Claims 3, 6-9 and 51 were rejected under 35 U.S.C. § 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter

which applicant regards as the invention." Applicants respectfully traverse this ground for rejection.

In particular, the Examiner rejected claim 3 stating that "it is unclear how an 'immunogenic fragment' would have 'immunological activity of carbonic anhydrase.'" Applicants have amended claim 3 to omit the phrase "an immunogenic fragment comprising at least about 10 amino acids of SEQ ID NO:1, wherein the fragment has immunological activity of carbonic anhydrase." Applicants request that the Examiner reconsider and withdraw the rejection.

VII. Claim Rejections – 35 U.S.C. § 102(b), previous

Claims 3, 6-7 and 9 were rejected under 35 U.S.C. § 102(b), as being allegedly anticipated by Lowe *et al.*, GENE, 93:277-283 (1990) ("Lowe"). Applicants respectfully traverse this ground for rejection.

The Examiner stated that "Claim 3 is directed to an immunogenic fragment comprising at least about 10 amino acids of SEQ ID NO: 1," and as such, the Examiner asserted that claims 3, 6-7 and 9 are anticipated by Lowe. Applicants have amended claim 3, from which claims 6-7 and 9 depend, to omit reference to "a biologically active fragment" or "an immunogenic fragment." As such, Applicants request that the Examiner reconsider and withdraw the rejection.

VIII. Claim Rejections – 35 U.S.C. § 102(e), new

Claims 3, 6-7 and 9 were rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by "Accession No. AAB59589 [USP 6160090, filing date 1993]." Applicants respectfully traverse this ground for rejection.

The Examiner stated that "Applicants' SEQ ID NO: 1, residues 191-207 are exact match to Accession No. AAB59589 residues 188-197, and reads on the claim 3 limitation 'of at least about 10 amino acids of SEQ ID NO: 1.'" Applicants have amended claim 3 to omit the limitation "of at least about 10 amino acids of SEQ ID NO: 1." As such, Applicants request that the Examiner reconsider and withdraw the rejection.

IX. Conclusion

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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